IN THE CLAIMS:

Claims 1-36 (Cancelled)

37. (Currently amended) A method of inhibiting a caspase which method comprises:

contacting the caspase with administering a compound of the structure:

wherein in Structure I

R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH-(R¹)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R¹ group is in the D or L configuration;

 R^2 is selected from the group consisting of

,)

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and together form a cyclic structure or a heterocyclic structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-0$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4;

$$-O$$
 (CH₂)_n-NH₂•X

wherein X is a salt, and n is 1-4; or

$$-0 \xrightarrow{R^7} = 0$$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl.

38. (Currently amended) A method of inhibiting apoptosis comprising administering a compound according to claim 1 to a human subject in need thereof for a time and under conditions effective to inhibit caspase; which method comprises contacting a caspase:

(a) a compound of the structure:

$$R^{5}$$
 R^{5}
 R^{5}
 R^{5}
 R^{5}
 R^{5}
 R^{5}
 R^{5}
 R^{6}
 R^{6}
 R^{6}

wherein in Structure I

R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R¹)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R^1 group is in the D or L configuration: R^2 is selected from the group consisting of

$$\frac{-F; \text{ and}}{R^4}$$

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro,

chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino, and together can form a cyclic ring structure in a heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-O$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4;

HO
$$- O - (CH2)n-NH2•X$$

where X is a, and n is 1-4;

$$-0 \xrightarrow{R^7} = 0$$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the acid or base salts thereof.

39. (Cancelled)

40. (Currently amended) The A method according to claim 38 for use as a protease inhibition, wherein

the method composition comprises administration of:

(a) a compound of the structure:

wherein in Structure I

R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R¹)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R¹ group is in the D or L configuration;

 R^2 is selected from the group consisting of

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino, and together can form a cyclic ring structure in a heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

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wherein A is a covalently bonded amine protecting group, and n is 1-4;

where X is a the pharmaceutically accepted salt, and n is 1-4;

$$-0 \xrightarrow{R^7} = 0$$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the pharmaceutically acceptable acid or base salts thereof, and

- (b) a pharmaceutically acceptable excipient.
- 41. (Previously presented) The method of Claim 40 wherein in the structure:

 R¹ is selected from isopropyl or isobutyl;

 R² is F; and R⁵ is hydrogen.
- 42. (Original) The method of Claim 40 wherein in the structure:R¹ is selected from isopropyl or isobutyl;R² is

$$-0$$

wherein R³ and R⁴ are each fluoro; and R⁵ is hydrogen.

43. (Previously presented) The method of Claim 42 wherein in the structure, R³ and

R⁴ in the 2 and 6 positions of the phenyl ring.

44. (Previously presented) The method of Claim 43 wherein R² is

$$-O$$
 $(CH_2)_nNH-A$

45. (Previously presented) The method of Claim 43 wherein R² is

$$-O$$
 $-(CH2)n-NH2•X$

46. (Previously presented) The method of Claim 43 wherein R² is

$$-0$$
 R^7
 $=0$

47. (Currently amended) The method of claim <u>38</u> 39 for use as a protease inhibitor as a composition,

wherein the compound composition comprises,

(a) a compound of the structure:

$$R^{5}$$

wherein R¹ is selected from the group consisting of methyl, ethyl, isopropyl, and iso-butyl;

R² is selected from the group consisting of:

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl having 1 to 10 carbon atoms, fluoro, chloro and amino;

and R⁵ and R⁵ are each selected from the group consisting of hydrogen having 1 to 10 carbon atoms, alkyl having 1 to 10 carbon atoms, alkoxyl having 1 to 10 carbon atoms, fluoro, and chloro;

$$-O - (CH2)n-NH2•X$$

wherein A is a covalently bonded amine protecting group, and n is 1-4;

$$-O$$
 (CH₂)_nNH-A

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wherein X is a pharmaceutically acceptable salt and n is 1-4;

$$-0$$

wherein R^7 is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl.

48. (Previously presented) The method of Claim 47 wherein R² is

$$-O$$
 (CH₂)_nNH-A

49. (Previously presented) The method of Claim 47 wherein R² is

$$-O$$
 $-(CH2)n-NH2·X$

50. (Previously presented) The method of Claim 47 wherein R² is

$$-0 \stackrel{R^{\dagger}}{\longleftrightarrow} = 0$$

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71. (Previously presented) The method of Claim 47, wherein in the structure:

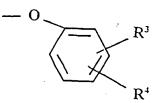
R¹ is selected from isopropyl or iso-butyl;

R² is -F; and

R⁵ is hydrogen.

52. (Previously presented) The method of Claim 47 wherein, in the structure R¹ is selected from isopropyl or isobutyl;

 R^2 is



wherein R³ and R⁴ are each fluoro; and R⁵ is hydrogen.

- 53. (Previously presented) The method of Claim 47 wherein in the structure, groups R³ and R⁴ are in the 2 and 6 positions of the phenyl ring.
- 54. (Currently amended) A method of Claim <u>39</u> 38 for use as an inhibitor to <u>for</u> caspase <u>inhibitor</u> or a caspase-like enzyme, which method <u>comprises</u> comprising using:
 - (a) a compound selected from the group consisting of:

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; and

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(b) a pharmaceutically acceptable excipient.

55. (Currently amended) A compound of the structure:

wherein in Structure III:

m is 1, 2 or 3, creating 1, 2 or 3 amino acid linkages, such that

when m = 1, $R^{A} = R^{1}$,

when m = 2, R^A is R^I and R^{IB} in the separate amino acids and

when m = 3, R^A is R^1 , R^{1B} and R^{1C} wherein R^1 , R^{1B} and R^{1C} in the separate amino acids which amino acids are the same or different amino acid when R^1 , R^{1B} and R^{1C} are independently selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R^1)-(C=O)-; N-CH(R^1)-(C=O)-NH-CH(R^{1B})-(C=O); or NCH(R^1)(C=O)-NH-CH(R^{1C})(C=O)-produces natural amino acid structures or an unnatural amino acid structures, and;

the carbon adjacent to R^1 group is in the D or L configuration; R^2 is selected from the group consisting of:

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro,

chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and together form a cyclic ring structure or a heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-O$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4, preferably 2;

where X is \underline{a} the pharmaceutically accepted salt, and n is 1-4, preferably 2; and

$$-0$$
 R'
 $=0$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the pharmaceutically acceptable acid or base salts thereof.

- 56. (Previously presented) The compound of Claim 55 wherein m = 2, R^1 and R^{1B} are each independently selected from methyl, ethyl, isopropyl and t-butyl.
- 57. (Previously presented) The compound of Claim 55 wherein m=3, R^1 , R^{1B} and R^{1C} are each independently selected from methyl, ethyl, isopropyl and t-butyl.

- 58. (Previously presented) The compound of Claim 57 wherein R² is F or 2,6-difluorophenoxy, R⁵ and R⁵ are each hydrogen and R⁶ is methyl.
- 59. (Currently amended) The protease A caspase inhibitor for use as a pharmaceutical as a composition comprising:

a compound selected from the structure:

wherein in Structure III:

m is 1, 2 or 3, creating 1, 2 or 3 amino acid linkages, such that

when m = 1, $R^A = R^I$,

when m = 2, R^A is R^1 and R^{1B} in the separate amino acids and

when m = 3, R^A is R^1 , R^{1B} and R^{1C} wherein R^1 , R^{1B} and R^{1C} in the separate amino acids which amino acids are the same or different amino acid when R^1 , R^{1B} and R^{1C} are independently selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R^1)-(C=O)-; N-CH(R^1)-(C=O)-NH-CH(R^{1B})-(C=O); or NCH(R^1)(C=O)-NH-CH(R^{1C})(C=O)- produces natural amino acid structures or an unnatural amino acid structures, and;

the carbon adjacent to R^1 group is in the D or L configuration; R^2 is selected from the group consisting of:

$$-0$$
 \mathbb{R}^3 $-F$; and

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and together form a cyclic ring structure or a heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-O$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4, preferably 2;

$$- O - (CH2)n-NH2•X$$

where X is the pharmaceutically accepted \underline{a} salt, and n is 1-4, preferably 2; and \mathbb{R}^7

wherein R^7 is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the pharmaceutically acceptable acid or base salts thereof; and a

pharmaceutically acceptable excipient.

- 60. (Currently amended) The pharmaceutical composition caspase inhibitor of Claim 59 wherein m = 2, R^1 and R^{1B} are each independently selected from methyl, ethyl, isopropyl and t-butyl.
- 61. (Currently amended) The pharmaceutical composition caspase inhibitor of Claim 59 wherein m=3, R^1 , R^{1B} and R^{1C} are each independently selected from methyl, ethyl, isopropyl and t-butyl.
- 62. (Currently amended) The pharmaceutical composition caspase inhibitor of Claim 59 wherein R² is F or 2,6-difluorophenoxy, R⁵ and R⁵ are each hydrogen and R⁶ is methyl.
- 63. (Currently amended) The pharmaceutical composition caspase inhibitor of Claim 62 wherein R² is F or 2,6-difluorophenoxy, R⁵ and R⁵ are each hydrogen and R⁶ is methyl.
- 64. (Currently amended) The method of treatment of claim 40 for a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, and spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:
- A. Administering a therapeutically an effective amount of the compound caspase inhibitor of claim 59.
- 65. (Currently amended) The method of treatment of claim 47 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and

neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

- A. Administering a therapeutically an effective amount of the compound caspase inhibitor of claim 60.
- 66. (Currently amended) The method of treatment of claim 53 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:
- A. Administering a therapeutically an effective amount of the compound caspase inhibitor of claim 61.
- 67. (Currently amended) The method of treatment of claim 54 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease; which method comprises:
- A. Administering a therapeutically effective amount of the compound of the caspase inhibitor of claim 60.
- 68. (Previously presented) The method of treatment of claim 59 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney

disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, <u>and</u> traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

- A. Administering a therapeutically an effective amount of the compound caspase inhibitor of claim 62.
- 69. (Currently amended) The method of treatment of claim 60 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, and traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:
- A. Administering a therapeutically an effective amount of pharmaceutical compositon of Claim 25 caspase inhibitor of claim 63.
 - 70. (Cancelled)